## REMARKS

Reconsideration in view of the above amendments and following remarks is respectfully requested. Claims 1-14 and 16-25 are pending in the instant application, with claims 1, 2, 4, 7, 10, and 22 being in independent form. Claims, 1, 4, 6-9, 23, and 25 were cancelled to simplify the issues, and to present the case for allowance under 37 CFR §1.116(a). The subject matter of these canceled claims will be pursued in a continuing application. The remaining claims are claims 2, 3, 5, 10, 22 and 24; claim 10 is allowable. The amendments to claims 3 and 5 were made to re-write claim 3 in independent format and to provide proper dependency of the claims; moreover, claim 3 and 5 were amended to provide claims of scope commensurate with the invention and to present the case for allowance under 37 CFR §1.116(a). The amendments to claims 22 and 24 were made to present the case for allowance under 37 CFR §1.116(a). Moreover these cancellations and amendments were made to focus on certain embodiments of the invention commensurate with business goals. The specification was amended to correct a typographical error. A marked-up version of the changes made to the specification and claims by the current amendment, "Explanation Of Amendments With Markings," is provided. An Appendix with the claim set including amended claims is provided for the Examiner's convenience, and shall not be construed as submission of a re-presented claim set under 37 CFR §1.121. No new matter was added by these amendments.

The specification was amended to correct a typographical error. The Phenylalanine that starts the mature sequence is located at position 22 rather than 23 in SEQ ID NO:2. The signal sequence is from amino acid 1 (Met) to 21 (Met) of SEQ ID NO:2 (see page 14, lines 11-15). SEQ ID NO:2 shows that the Phe is at position 22 rather than 23. As such, this error is supported in the specification as filed, and correction thereof presents no new matter.

Applicant notes that claim 10 in the response to the previous Office Action (October 25, 2000) Amendment and Appendix was unintentionally stated in error (see page 3, and 17 of the October 25 Response). In the Response, in discussing amendments to claim 10, the claim is correctly stated (see page 13 of the October 25 Response). The signal sequence of z219c is from amino acid 1 (Met) to 21 (Met) of SEQ ID NO:2 (see page 14, lines 11-15; and page 34

lines 2-4; and original claim 10). Applicant had not formerly amended this in the October 25 response, so has not marked it as amended in the instant response. However, Applicant desires to point out to the Office that this error occurred, and to clarify the record and any confusion it may have created. The claim 10 of the instant response is properly stated without error, and there is no new matter presented in correcting this error.

Claim 3 was amended to re-write the claim in independent format so it does not depend on a canceled claim. Moreover, in addition to including the full length cDNA (nucleotide 1 to nucleotide 699 of SEQ ID NO:8; corresponding to nucleotide 222 to nucleotide 890 of SEQ ID NO:1), the claim was amended to include a cDNA fragment corresponding to the mature form (nucleotide 64 to nucleotide 699 of SEQ ID NO:8; corresponding to nucleotide 285 to nucleotide 890 of SEQ ID NO:1). Support for the inclusion of this fragment in the claim can be found in original claim 2; SEQ ID NO:1; SEQ ID NO:8; page 14, lines 1-17; and page 16, lines 11-21. One of skill in the art upon reading the specification would readily recognize that nucleotide 222 to nucleotide 890 of SEQ ID NO:1, corresponds to nucleotide 64 to nucleotide 699 of SEQ ID NO:8. Claim 5 was similarly amended, and is a narrower embodiment within the scope of the invention, and depends from claim 3. No new matter was added by these amendments.

Similarly, independent claim 22 was amended to provide for vectors generally, rather than expression vectors. The amendments also removed the reference to the z219c polypeptide of SEQ ID NO:2 in the "DNA segment" and rather includes the corresponding full length and mature cDNA fragments as described by SEQ ID NO:1 and SEQ ID NO:8 instead, as supported in the specification as described above. In addition claim 24, is now drawn to a "cell", rather than a "cultured cell" and no longer contains the limitation that the polypeptides are expressed by the vector, since this limitation is not essential for the amplification of useful DNA fragments encompassed by certain embodiments of the invention, such as chromosomal probes. No new matter was added by these amendments.

***A. Rejections Addressed from January 17 Office Action (OA)***

***(1) Rejection of claims 1-9 and 22-25 under 35 U.S.C. §101***

Claims 1-9 and 22-25 were rejected under 35 U.S.C. §101 because the claimed invention "is not supported by either a specific asserted utility or well established utility." (OA, p. 2) To expedite prosecution of the case toward allowance, Applicant has canceled claims 1, 4, 6-9, 23 and 25 and as such this rejection is moot as applied thereto. Moreover, Applicant has amended claims 3, 5, and 22 and 24 to expedite prosecution. Applicant respectfully traverses this rejection as it applies to remaining claims 2, 3, 5, 22 and 24.

To be considered useful under 35 U.S.C. §101, an invention must have a specific, substantial and credible utility. It is well established "when a properly claimed invention meets at least one stated objective, utility under §101 is clearly shown." (*Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958 (CAFC 1983)). That is, only a single utility for an invention needs be disclosed in a patent application to satisfy the 35 U.S.C. §101 utility requirement.

In making this rejection the Office states:

> Applicants argue that the polynucleotides of the invention constitute probes that have a diagnostic utility due to their chromosomal localization at 3q21.1-p13....[T]he invention spans over a quite large fragment of chromosome 3 (3q21.1-p13 region of chromosome 3) and no specific localization is provided allowing determination of where the probe actually hybridizes, and if the site corresponds to a marker for a specific disease characterized, for example by a specific deletion or mutation....There is no evidence that LOH (loss of heterozygosity) is associated with the polynucleotide of the present invention....although chromosomal deletions and translocations are associated with various tumors (see for example Cigurosa...there is no nexus between the claimed nucleid acid and any known deletion, nor sufficient information to allow the use of the claimed nucleic acid for the detection of any deletion or other alteration associated with any known tumor or other condition. (OA, p. 3-4)

Applicant respectfully disagrees with this contention as the specification has indeed asserted utility. One of skill in the art upon reading the specification would immediately appreciate that the polynucleotides of the present invention are located at a specific chromosomal location wherein translocations are associated with human disease; and would immediately appreciate that the polynucleotides could serve as a useful diagnostic for detecting and analyzing translocations and other genetic abnormalities at that locus. As such, one of skill in the art would immediately appreciate that the polynucleotides of the present invention have specific and well-

established utility. Moreover, the Office has presented no evidence to refute such assertions of utility.

The instant claims are drawn to inventive polynucleotides. As disclosed in the specification, from page 71, line 33 to page 74, line 7, the polynucleotides of the present invention can serve as diagnostics for human chromosome 3 abnormalities, particularly at the specific locus where the z219c gene is located, 3p21.1-p13. As further disclosed in the specification and known by one of skill in the art, applicant emphasizes that translocation and loss of heterogeneity (LOH) at the specific 3p21.1-p13 locus are gross chromosomal abnormalities that clearly associated with human disease, such as cancers (e.g., see page 73, lines 7-35, and references of record), and hence the polynucleotides of the present invention can be used specifically as a diagnostic. Contrary to the beliefs of the Office, LOH and translocations associated with cancers occur at this locus, and Applicant has indeed asserted a specific utility for the polynucleotides of the present invention as a chromosomal marker and probe. Moreover, it is well settled in the art how to use such polynucleotides as probes to detect and analyze chromosomal aberrations in the 3p21.1-p13 region of chromosome 3 is discussed and enabled in the specification (page 71, line 33 to page 74, line 7). Moreover, said utility is substantial and credible, as it is well known in the art that diagnostics for genetic diseases and tumors are sought after, and they are currently used in present day medicine to diagnose genetic disease or malignancy, or carriers or those susceptible to genetic disease, or to assist physicians in analyzing disease.

The Office is concerned that the instant chromosomal localization for the polynucleotides of the present invention is not specific enough to be useful, because it spans what the Office considers a reasonably large section of chromosome 3, 3p21.1-p13. However, it is clearly evident, and one of skill in the art would at the time of filing would recognize that chromosomal abnormalities such as translocations and loss in the 3p21.1-p13 locus are evident in many human tumors, and that this locus of chromosome 3 is a hot-spot wherein translocations and LOH within 3p21.1-p13 are evident in tumors and malignancy in humans. It is well known that such translocations are between entire chromosomes, that is, they are gross chromosomal abnormalities. Hence z219c polynucleotide probes can serve as a diagnostic for such chromosomal aberrations (as described in the specification page 71, line 33 to page 74, line 7),

and aid in diagnosis of human cancers. Moreover, one of skill in the art would recognize that of z219c polynucleotide probes are particularly useful for diagnosis of gross chromosomal abnormalities associated with loss of heterogeneity (LOH), translocation, rearrangements, chromosome gain (e.g. trisomy), DNA amplification, and the like. Such uses for the polynucleotides of the present invention are described in the specification (page 72 lines 12-30). Translocations, deletions and LOH within chromosomal locus 3q21.1-p13 wherein the z219c gene is located were known at the time of filing to be associated with human disease, and research has continued to show that this locus is involved in human disease. Upon reading the specification, these uses would be apparent to one of skill in the art, in spite of whether the polynucleotides of the present invention span a reasonably large section of chromosome 3, 3p21.1-p13.

The Office incorrectly states that "There is no evidence that LOH (loss of heterozygosity) is associated with the polynucleotide of the present invention....although chromosomal deletions and translocations are associated with various tumors (see for example Cigurosa...there is no nexus between the claimed nucleic acid and any known deletion, ... deletion or other alteration associated with any known tumor or other condition. (OA, p. 4). However, Applicant has presented evidence in the specification and described herein, and has clearly disclosed in the specification that LOH and translocations within 3q21.1-p13 are associated with several human cancers and hence z219c polynucleotides within this locus are useful. For example, Shridhar, V. et al, Oncogene, 12:1931-1939, 1996, cited in the specification, show that chromosome 3p breakage, translocation and LOH at 3p14 is common in renal cell carcinomas, including nonpapillary, papillary and oncocytomas. Moreover, other aberrations within 3q21.1-p13 are associated with cancers, for example: mylodysplastic syndrome and acute myeloid leukemia (3p21 is recurrent treatment-related breakpoint, Shi, G et al,. Cytogenet. Cell Genet. 74:295-299, 1996); human carcinomas (3p21.3 LOH, Imreh, S et al. Genes Chromosomes Cancer 20:224-233, 1997); hereditary renal cell carcinoma (3p14 translocation breakpoint and loss, Shridhar, R. et al, Cancer Res., 56:5576-5578, 1996 cited in specification); malignant development to clear cell or nonpapillary renal cell carcinoma (losses of 3p21 necessary, Vand den Berg, A et al., Genes Chromosomes Cancer. 15:64-72, 1996, Vand den Berg, A, and Buys, CH Genes Chromosomes Cancer. 19:59-76, 1997); human lymphoid

neoplasms (3p21 breakpoints and deletions, Cigudosa, JC et al. Genes Chromosomes Cancer. 25:123-133, 1999); renal cell carcinoma (3p12-14 translocation and 3p21.2-21.3 deletion, Clifford, SC et al. Genes Chromosomes Cancer. 22:200-209, 1998); malignant lymphomas ((3;11)(p21;q23) translocation; Diabata, M. et al. Cancer Genet. Cytogenet. 117:28-31, 2000). Copies of the references above were previously provided for the Examiner's convenience, and are of record. It is clear, and it would have been at the time of filing, that the 3q21.1-p13 locus would be immediately appreciated by one of skill in the art as a critical region for translocations involved in human malignancies and tumors. As such, one of skill would immediately appreciate that polynucleotide probes as markers within this locus, such as the z219c polynucleotides of the present invention, are useful for detecting and analyzing translocations and LOH involved in human malignancies and tumors. Translocations, deletions and LOH within chromosomal locus 3q21.1-p13 wherein the z219c gene is located were known at the time of filing to be associated with human disease, and research has continued to show that this locus is involved in human disease. Upon reading the specification, these uses would be apparent to one of skill in the art, that in spite of whether the polynucleotides of the present invention might span a reasonably large section of chromosome 3 (i.e., 3p21.1-p13) there is a clear nexus between 3q21.1-p13 translocations, for instance, and human disease. Applicant has provided evidence that gross chromosomal abnormalities in and around 3p21.1-p13 are clearly associated with human disease, and hence shown that the polynucleotides of the present invention are supported by a specific asserted utility that is substantial and credible

The Office has not appreciated that the polynucleotides of the present indeed map to a specific site that is useful for the purposes of 35 USC §101. That specific site is 3p21.1-p13. The Office has presented no evidence to demonstrate that a gene that spans a reasonably large section o f human chromosome 3, i.e., 3p21.1-p13 would not have specific utility as a marker for the 3p21.1-p13 region. In making the rejection, the Office believes that "for chromosomal markers to be specific, they have to map to a specific site, which is supported by the fact that researchers usually need a set of closely spaced markers to assess...an interstitial break (Shridhar, 1997)." (OA, p.4) Closely spaced markers may be desirous to determine a precise chromosomal breakpoint; but to assess a translocation, markers are not considered useless by a skilled artisan if they are not so closely spaced. Shridhar, 1997 shows "considerable breakage and loss of 3p

sequences in RCC and possibly many other cancers." And goes on to state that "closely spaced markers enabl[e] one to properly assess the interstitial breaks *more precisely*." (Shridhar, 1997, page 1271, column 2, emphasis added). In fact, the Shridhar paper builds on past useful translocation data with other less closely spaced markers that previously showed interstitial breaks within 3p, by using more closely spaced markers to more precisely define the translocation breakpoint. The Shridhar reference does not state that closely spaced markers are *essential* to show utility in a chromosomal marker, or to detect a translocation generally. In fact, the Office has presented absolutely no evidence to show that the polynucleotides of the present invention could not be used as chromosome 3p21.1-p13 markers to diagnose 3p21.1-p13 translocations. In fact, karyotyping, a gross microscopic analysis to detect gross chromosomal abnormalities, is still considered a useful diagnostic in the art (see, Diabata, 2000, of record, page 29, showing translocation at 3p21 in lymphoma). It is unreasonable for the Office to believe that a more precise method, such as using the polynucleotides of the present invention as chromosomal probes within 3p21.1-p13, would be considered non-useful by a skilled artisan. The Office has presented no evidence to refute the assertions of utility as a 3p21.1-p13 chromosomal probe. Moreover, as detailed above, Applicant has provided evidence that gross chromosomal abnormalities within 3p21.1-p13, such as translocations, are clearly associated with human disease, and hence shown that the polynucleotides of the present invention are supported by a specific asserted utility that is substantial and credible.

Thus, since the z219c gene maps to this critical region involved in human malignancy and tumors, z219c polynucleotide probes of the present invention can be used to detect abnormalities or genotypes associated with 3q21.1-p13 translocation, deletion LOH, and the like, described above. Moreover, the specific utility of z219c polynucleotides to detect such large chromosomal aberrations is clearly described in the specification at pages page 71, line 33 to page 74, line 7 and more specifically at. 72 line 12-30. Moreover, this utility is asserted and is well-established, as one of ordinary skill would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., because of the property of these polynucleotides having a 3q21.1-p13 chromosomal localization).

Claims 2, 3, 5, 22 and 24 are indeed supported by a specific asserted utility that is substantial and credible. This is all 35 U.S.C. §101 requires. Consequently, the rejection of claims 2, 3, 5, 22 and 24 should be properly withdrawn.

***(2) Rejection of claims 1-9, and 22-25 under 35 U.S.C. §112, First Paragraph***

Claims 1-9 and 22-25 were rejected under 35 U.S.C. §112, First Paragraph because "since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention." (OA, p. 4). To expedite prosecution of the case toward allowance, Applicant has canceled claims 1, 4, 6-9, 23 and 25, and as such this rejection is moot as applied thereto. Moreover, Applicant has amended claims 2, 3, 5, 22 and 24 to expedite prosecution. Applicant respectfully traverses this rejection as it applies to remaining claims 2, 3, 5, 22 and 24.

As discussed in Part A(1) above, Applicant has indeed asserted a specific and well established utility for the useful polynucleotides of the present invention. Claims 2, 3, 5, 22 and 24 are indeed supported by a specific asserted utility that is substantial and credible, and as such, the Office has no basis for the instant rejection under 35 U.S.C. §112, First Paragraph. Moreover, claim 5, which depends from claim 3 is drawn to polynucleotides of the present invention, as shown in SEQ ID NO:8. The polynucleotides of the present invention are useful chromosome 3p21.1-p13 probes, and the Office has not presented evidence to refute that utility. It is well known in the art that a polynucleotide of the present invention would not have to be identical in sequence to SEQ ID NO:1 to serve as a probe to hybridize to a target sequence, e.g., human chromosomal DNA at locus 3p21.1-p13, since degenerate sequences such as SEQ ID NO:8 and fragments thereof and polynucleotide probes are commonly used to isolate and identify non-identical polynucleotide sequences such as allelic variants, and orthologs (e.g., see, page 16, line 11 to page 19, line 11; and page 22 line 12 to page 23, line 29), and DNA fragments or PCR are often used to probe chromosomes for gross defects, such as translocations and LOH, and to determine chromosomal localization (e.g., see, page 71, line 33 to page 74, line 35, and Example 3). That is, one of skill in the art would have a reasonable expectation of success that the polynucleotides of the present invention shown in SEQ ID NO:1 and SEQ ID NO:8 and fragments thereof could be used detect human chromosomal abnormalities associated with

disease, and particularly translocations associated with cancers, that are shown to be prevalent within the specific 3p21.1-p13 locus wherein the polynucleotides of the present invention will detect. In addition, expression vectors and cultured cells (e.g., claims 22, and 24) are routinely used in the art to generate copies or provide templates of the polynucleotide sequences of the present invention, e.g., to be subsequently isolated as polynucleotide probes. One of skill in the art would know how to make and use the invention, and the specification teaches one of skill in the art to do so. As such, the Office has no basis for the instant rejection under 35 U.S.C. §112, First Paragraph.

The teachings of the specification are commensurate with the scope of the claims. Upon reading the specification and claims, one of skill in the art can make and use polynucleotides of the present invention, without undue experimentation. This is all 35 USC 112, First Paragraph, requires. Consequently, the rejection of claims 2, 3, 5, 22 and 24 under 35 U.S.C. §112, First Paragraph, should be properly withdrawn.

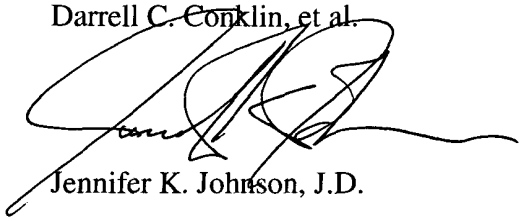
*(3) General lack of evidence and support in making rejections.*

Furthermore, Applicant respectfully emphasizes that no argument by the Office has been supported, nor data or evidence been cited or presented by the Office in making the instant rejections, aside from those apparent facts that are based on the personal knowledge of an employee of the Office, i.e., the Examiner. Applicant is hereby respectfully requesting the Examiner to provide an affidavit under 37 CFR §1.104(d)(2) which states: "When a rejection in an application is based on facts within the personal knowledge of an employee of the Office, the data shall be as specific as possible, and the reference must be supported, when called for by the applicant, by the affidavit of such employee, and such affidavit shall be subject to contradiction or explanation by the affidavits of the applicant and other persons."

Early reconsideration and allowance of the pending claims is respectfully requested. If the Patent Examiner believes that a telephone interview would expedite prosecution of this patent application, please call the undersigned at (206) 442-6676.

Respectfully Submitted,

Darrell C. Conklin, et al.



Jennifer K. Johnson, J.D.

Registration No. 43,696

Enclosures:

Amendment Fee Transmittal (in duplicate)

Petition and Fee for 3 Month Extension of Time (in duplicate)

Notice of Appeal

Explanation of Amendments with Markings (4 pages)

Appendix (2 pages)

Postcard

**EXPLANATION OF AMENDMENTS WITH MARKINGS TO SHOW CHANGES MADE**

IN THE SPECIFICATION

On page 14, the paragraph starting on line 11, please replace with the following paragraph:

Analysis of the DNA encoding z219c polypeptide (SEQ ID NO:1) revealed an open reading frame encoding 223 amino acids (SEQ ID NO:2) comprising a predicted signal peptide of 21 amino acid residues (residue 1 (Met) to residue 21 (Met) of SEQ ID NO:2), and a mature polypeptide of 194 amino acids (residue ~~23~~ 22 (Phe) to residue 223 (Phe) of SEQ ID NO:2). Multiple alignment of z219c with other members of the human 2-19 protein family revealed the following 3 regions of conserved amino acids (see Figure):

IN THE CLAIMS

Please cancel claims 1, 4, 6, 7, 8, 9, 23, and 25 without prejudice to the prosecution thereof on a subsequent application:

~~1. An isolated polynucleotide that encodes a polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:~~

~~(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 23 (Phe), to amino acid number 223 (Phe); and~~

~~(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 223 (Phe).~~

~~4. An isolated polynucleotide that encodes a polypeptide comprising a sequence of amino acid residues from the group consisting of:~~

~~(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 23 (Phe), to amino acid number 223 (Phe); and~~

~~(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 223 (Phe).~~

~~6. The isolated polynucleotide molecule of claim 1, wherein the polynucleotide encodes a polypeptide that contains motifs 1, 2, 3, 4 and 5 spaced apart from N-terminus to C-terminus in a configuration M1-{25-26}-M2-{15}-M3-{11}-M4-{34-36}-M5.~~

~~wherein M1 is "motif 1," a sequence of amino acids as shown in amino acids 118 to 120 of SEQ ID NO:2,~~

~~M2 is "motif 2," a sequence of amino acids as shown in amino acids 146 to 148 of SEQ ID NO:2,~~

~~M3 is "motif 3," a sequence of amino acids as shown in amino acids 164 to 166 of SEQ ID NO:2,~~

~~M4 is "motif 4," a sequence of amino acids as shown in amino acids 178 to 180 of SEQ ID NO:2, and~~

~~M5 is "motif 5," a sequence of amino acids as shown in amino acids 215 to 217 of SEQ ID NO:2, and~~

~~{#} denotes the number of amino acids between the motifs.~~

~~7. An expression vector comprising the following operably linked elements:~~

~~a transcription promoter;~~

~~a DNA segment encoding a polypeptide that is at least 90% identical to an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 23 (Phe), to amino acid number 223 (Phe); and~~

~~a transcription terminator,~~

~~wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.~~

~~8. An expression vector according to claim 7, further comprising a secretory signal sequence operably linked to the DNA segment.~~

~~9. A cultured cell into which has been introduced an expression vector according to claim 7, wherein the cell expresses the polypeptide encoded by the DNA segment.~~

~~23. An expression vector according to claim 22, further comprising a secretory signal sequence operably linked to the DNA segment.~~

~~25. A method of producing a polypeptide comprising:~~
~~culturing a cell according to claim 24; and~~
~~isolating the polypeptide produced by the cell.~~

Please amend the claims as follows:

3. (Amended) An isolated polynucleotide sequence ~~according to claim 1, wherein the polynucleotide~~ that comprises nucleotide 1 to nucleotide 669 or nucleotide 64 to nucleotide 699 of SEQ ID NO:8.

5. (Twice Amended) An isolated polynucleotide according to claim 3 ~~4~~, wherein the polynucleotide ~~encodes a polypeptide that~~ consists of nucleotide 1 to nucleotide 699 or nucleotide 64 to nucleotide 699 of SEQ ID NO:8 ~~a sequence of amino acid residues as shown in SEQ ID NO:2 from amino acid number 23 (Phe), to amino acid number 223 (Phe).~~

22. (Amended) ~~An expression~~ A vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment ~~encoding a polypeptide~~ comprising a polynucleotide selected from the group consisting of:

(a) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 285 to nucleotide 890;

(b) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:1 from nucleotide 222 to nucleotide 890;

(c) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 1 to nucleotide 699;

(d) polynucleotide molecules comprising a nucleotide sequence as shown in SEQ ID NO:8 from nucleotide 64 to nucleotide 699; and

(e) polynucleotide molecules complementary to (a), (b), (c) or (d) ~~an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 23 (Phe), to amino acid number 223 (Phe)~~; and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

24. (Amended) A ~~cultured~~ cell into which has been introduced ~~an expression~~ a vector according to claim 22~~, wherein the cell expresses the polypeptide encoded by the DNA segment~~.